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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/516,777	01/13/2006	Jochim Luthle	Le A 36 131	5263
<div>35969759001/15/2010 Barbara A. Shimei Director, Patents & Licensing Bayer HealthCare LLC - Pharmaceuticals 555 White Plains Road, Third Floor Tarrytown, NY 10591</div>				
EXAMINER				
MABRY, JOHN				
ART UNIT		PAPER NUMBER		
1625				
MAIL DATE		DELIVERY MODE		
01/15/2010		PAPER		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/516,777

Applicant(s)

LUITHE ET AL.

Examiner

JOHN MABRY

Art Unit

1625

Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on November 10, 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-13, 15 and 19 is/are pending in the application.
- 4a) Of the above claim(s) 12, 13 and 19 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-11 and 15 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB06)
- 4) ☐ Interview Summary (PTO-413)
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____
- Paper No(s)/Mail Date 12/02/04.

DETAILED ACTION

Examiner's Response

Applicant's response on November 10, 2009 filed in response to the Election/Restriction dated December 23, 2008 has been received and duly noted. The Examiner acknowledges Applicant's election of Group I with traverse. The Applicant requested the rejoinder of Groups III and IV to examine along with elected Group I because Applicant's allegation that it would not be an undue search burden. According to restriction practice as required under 35 USC 121, 372 and PCT Rule 13.01, Applicant's unity of invention was properly broken, thus the invention was properly restricted. However, to address Applicant's arguments of no undue search burden, the following evidence is respectfully set forth.

During the search of an elected group, a class/subclass search must be made (according to the US Patent Examination process). Group I is classified in class/subclass 549/57. Group IV method claims, as it regards to Group I, would be classified in class/subclass 514/443. EAST search results (shown below), shows that 549/57 results in 497 references in which Examiner has to search and 1,317 references for 514/443. This clearly shows evidence that it would be an undue search burden if Examiner had to search these two groups simultaneously.



Active

L3: (497) 549/57 ccls.

L4: (1,317) 514/443 ccls.

When the elected compounds claims become allowance, the Examiner will rejoin a process of making and a method of using which corresponds the limitations of the elected compound group.

Thus, the restriction requirement is deemed proper and **FINAL**.

In view of this response, the status of the rejections/objections of record is as follows:

Foreign Priority

Acknowledgment is made of applicant's claim for foreign priority based on applications filed as shown below:

10305922.9 02/13/2003 GERMANY

10257537.1 12/10/2002 GERMANY

10257078.7 12/06/2002 GERMANY

10225536.9 06/10/2002 GERMANY

PCT/EP03/05735 06/02/2003

It is noted, however, that applicant has not filed a certified English translation of the above applications as required by 35 U.S.C. 119(b).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-11 and 15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for salts, does not reasonably provide enablement for solvates, solvates of a salt or hydrates. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The claims are drawn to solvates and solvates of a salt. But the numerous examples presented all failed to produce a hydrate or solvate. These cannot be simply willed into existence. As was stated in *Morton International Inc. v. Cardinal Chemical Co.*, 28 USPQ2d 1190 "The specification purports to teach, with over fifty examples, the preparation of the claimed compounds with the required connectivity. However ... there is no evidence that such compounds exist... the examples of the '881 patent do not produce the postulated compounds... there is ... no evidence that such compounds even exist." The same circumstance appears to be true here: there is no evidence that solvates of these compounds actually exist; if they did, they would have formed. Hence, applicants must show that solvates can be made, or limit the claims accordingly.

Claims 1-11 and 15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for E being C≡C and arylene where arylene is phenyl and heteroarylene is pyridinyl, pyrimidinyl, thiophenyl, pyrrolyl, oxadiazolyl, but does not reasonably provide enablement for E being all arylene and heteroarylene chemical moieties as claimed.

R⁴ is hydrogen, halogen, cyano, amino, trifluoromethyl, trifluoromethoxy, C₁-C₆-alkyl, C₁-C₆-alkylcarbonyl, C₁-C₆-alkylamino, formyl, hydroxycarbonyl, C₁-C₆-alkoxy, C₁-C₆-alkoxycarbonyl, C₃-C₆-alkylthio, C₃-C₆-alkylcarbonylamino, C₁-C₆-alkylaminocarbonyl, C₁-C₆-alkylsulfonylamino, C₃-C₆-cycloalkylcarbonylamino, C₃-C₆-cycloalkylaminocarbonyl, pyrrolyl, C₁-C₆-

does not reasonably provide enablement for R4 being all claimed heterocyclylcarbonyl, heterocyclylcarbonylamino, heteroaryl amino and heterocyclyls where C1-C6 alkyls are optionally substituted by all claimed heterocyclyl and all claimed C1-C6alkylcarbonylamino are optionally substituted by all claimed heterocyclyl substituents.

Pursuant to *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), one considers the following factors to determine whether undue experimentation is required: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. Some experimentation is not fatal; the issue is whether the amount of experimentation is "undue"; see *In re Vaeck*, 20 USPQ2d 1438, 1444.

The analysis is as follows:

(1) Breadth of claims: Scope of the compounds. Owing to the range of many variables, millions of highly substituted benzofuranyl and benzothiofuranyl compounds are embraced.

(2) The nature of the invention: The invention is a highly substituted benzofuranyl and benzothiofuranyl compounds.

(3) Level of predictability in the art: It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and chemical reactivity (which is affected by determinants such as substituent effects, steric effects, bonding, molecular geometry, etc) is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

(4) Direction or Guidance: That provided is very limited. Applicant shows a general synthesis of compounds of application's general formula I. Pages 40-67 of the Specification describes starting materials and methods for synthesis of compounds wherein E and R4 as aforementioned, but does not describe or list any reagents wherein compounds can be used to synthesis compounds where E and R4 as listed above. There is limited evidence in the Specification of the example compounds that only covers no or a small portion of the substituents claimed of formula. Thus, there is no specific direction or guidance regarding said compounds specifically mentioned in Scope.

For instance, Applicant claims the following terms: heterocyclyl- and heteroarylene (see definitions are defined in Specification below – pages 8 and 9 below). The specification does not provide any support for the synthesis of compounds, wherein E and R4 as shown below.

Heteroaryl is an aromatic, mono- or bicyclic radical having 5 to 10 ring atoms and up to 5 heteroatoms from the series S, O and/or N. Preference is given to 5- to 6-membered heteroaryls having up to 4 heteroatoms. The heteroaryl radical may be bonded via a carbon atom or heteroatom. Nonlimiting examples include: thienyl, furyl, pyrrolyl, thiazolyl, oxadiazolyl, oxazolyl, isoxazolyl, imidazolyl, tetrazolyl, pyridyl, pyrimidinyl, pyridazinyl, indolyl, indazolyl, benzofuranyl, benzothiophenyl, quinolinyl, isoquinolinyl.

Heterocycliccarbonylamino is a carbonylamino group which is linked to a mono- or polycyclic, preferably mono- or bicyclic, nonaromatic radical having, as a rule, 4 to 10, preferably 5 to 8, ring atoms and up to 3, preferably up to 2, hetero ring members from the series N, O, S, SO, SO₂. The heterocyclyl radicals may be saturated or partially unsaturated. Nonlimiting examples include carbonylamino groups linked to 5- to 8-membered monocyclic saturated heterocyclyl radicals having up to two hetero

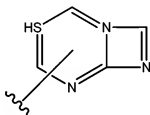
ring atoms from the series O, N and S such as tetrahydrofuran-2-ylcarbonylamino, piperazinylcarbonylamino, N-methylpiperazinylcarbonylamino, pyrrolidin-2-ylcarbonylamino, pyrrolidin-3-ylcarbonylamino, pyrrolinylcarbonylamino, piperidinylcarbonylamino, morpholinylcarbonylamino and perhydroazepinylcarbonylamino.

Heteroarylcarbonylamino is a carbonylamino group which is linked to a mono- or bicyclic aromatic radical having 5 to 10 ring atoms and up to 5 heteroatoms from the series S, O and/or N. Preference is given to 5- to 6-membered heteroaryls having up to 4 heteroatoms. The heteroaryl radical may be bonded to the carbonylamino group via a carbon atom or heteroatom. Nonlimiting examples include: thienylcarbonylamino, furylcarbonylamino, pyrrolylcarbonylamino, thiazolylcarbonylamino, isoxazolylcarbonylamino, oxadiazolylcarbonylamino, oxazolylcarbonylamino, imidazolylcarbonylamino, tetrazolylcarbonylamino, pyridylcarbonylamino, pyrimidinylcarbonylamino, pyridazinylcarbonylamino, indolylcarbonylamino, indazolylcarbonylamino, benzofuranylcarbonylamino, benzothienophenylcarbonylamino, quinolinylcarbonylamino, isoquinolinylcarbonylamino.

Heterocyclylcarbonyl is a carbonyl group which is linked to a mono- or polycyclic, preferably mono- or bicyclic, nonaromatic radical having, as a rule, 4 to 10, preferably 5 to 8, ring atoms and up to 3, preferably up to 2, hetero ring members from the series N, O, S, SO, SO₂. The heterocyclyl radicals may be saturated or partially unsaturated. Nonlimiting examples include carbonyl groups linked to 5- to 8-membered monocyclic saturated heterocyclyl radicals having up to two hetero ring atoms from the series O, N and S such as tetrahydrofuran-2-ylcarbonyl, piperazinylcarbonyl, N-methylpiperazinylcarbonyl, pyrrolidin-2-ylcarbonyl, pyrrolidin-3-ylcarbonyl, pyrrolinylcarbonyl, piperidinylcarbonyl, morpholinylcarbonyl and perhydroazepinylcarbonyl.

Examiner respectfully acknowledges examples shown in the Specification and guidance provided, but that does not mean that Applicant is enabled for the entire claimed invention. Applicant's very few exemplified examples does not automatically enable Applicant for the entire scope of this claimed terms. For instance, Applicant

claims the term heteroaryl in the specified variables above. According to the Specification the following bicyclic heteroaryl compound is claimed below. A preliminary search results, STN Structure database shows that these compounds do not exist. Additionally, this compound cannot be purchase from Sigma-Aldrich (nor can reagents), in order synthesized compounds of claimed Formula I. Applicant has not provided such guidance thus is not enabled to make compounds of the full scope as claimed.



There is limited evidence in the Specification of the example compounds that only covers no or a small portion of the substituents claimed of formula.

The availability of the starting material that is needed to prepare the invention as claimed is at issue here...As per MPEP 2164.01 (b). A key issue that can arise when determining whether the specification is enabling is whether the starting materials or apparatus necessary to a make the invention are available. In the biotechnical area, this is often true when the product or process requires a particular strain of microorganism and when the microorganism is available only after extensive screening. The Court in *re Ghiron*, 442 F.2d 985, 991, 169 USPQ 723, 727 (CCPA 1971), made it clear that if the practice of a method requires a particular apparatus, the application must provide a sufficient disclosure of the apparatus if the apparatus is not readily available. The same can be said if certain chemicals are required to make a compound

or practice a chemical process. *In re Howarth*, 654 F.2d 103, 105, 210 USPQ 689, 691 (CCPA 1981).

It is not trivial to experimentally interchange any and all of the many substituents that exist. As generally described by F. Zaragoza Dörwald, most organic syntheses fail initially and chemical research is highly inefficient due to chemists spending most of their time "finding out what went wrong and why". Therefore, most syntheses of organic compounds are labor-intensive and demanding. Additionally, most final synthetic routes to desired organic molecules are usually very different from initially planned routes. A highly skilled chemist can agree that for many successful organic compounds made, many failures are encountered and experimental repetition is common. This also contributes to the burden and unpredictability of the syntheses of said compounds. (see "Side Reactions in Organic Synthesis: A Guide to Successful Synthesis Design" 2005 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim.

(6) Working Examples: Applicant shows examples in Specification but no working examples were shown wherein E and R4 equal aforementioned substituents have been made or used of any kind.

(7) Skill of those in the art: The ordinary artisan is highly skilled, e.g. a masters or PhD level chemist.

(8) The quantity of experimentation needed: Since there are very limited working examples as described above, the amount of experimentation is expected to be high and burdensome.

Due to the level of unpredictability in the art, the very limited guidance provide, and the lack of working examples, the Applicant has not provided sufficient guidance for the artisan to make the invention.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.

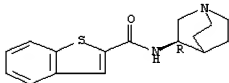
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-9 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over 10/500,096 (US 20050119325 which has a PCT (WO 03/055878 – PTO-1449) filing date of December 16, 2002).

The instant application claims compounds and pharmaceutical compositions of Formula I, wherein A=S, O and ring B = benzo, E=phenyl, R₃=H and R₄=H.

Scope & Content of Prior Art MPEP 2141.01

10/500,096 discloses compounds and pharmaceutical compositions of Formula I, wherein A=S, O and ring B = benzo (see Example 51, page 108 of Specification).



Differences between Prior Art & the Claims MPEP 2141.02

The instant application and 10/500,096 differs at variable E: Applicant's phenyl versus 10/500,096's H. However, 10/500,096 teaches that ring B = benzo where benzo is substituted by benzo (see page 3, line 12 of the Specification). The substituted benzo represents E=phenyl and R₄=H of the instant application.

The closest definition found in the Specification of 10/500,096 regarding the term "benzo" is found of page 6 of its Specification where the term phenylcarbonyl radical

corresponds to benzoyl radical. In essence, 10/500,096 equates the term benzo to mean phenyl. In the chemical community, the term "benzo" is commonly referred and related to the term "phenyl".

Prima Facie Obviousness, Rational & Motivation MPEP 2142-2413

It would be obvious for an skilled artisan to replace the compound(s) as shown by 10/500,096 along with its teaching in order to achieve the instantly claimed invention as clearly explained above.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thornton*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-9 and 15 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6, 11, 16-21 and 23 of copending Application No. 10/500,096. Although the conflicting claims are not identical, they are not patentably distinct from each other because of the following.

The instant application claims compounds and pharmaceutical compositions of Formula I, wherein A=S, O and ring B = benzo, E=phenyl, R3=H and R4=H.

10/500,096 claims compounds and pharmaceutical compositions of Formula I, wherein A=S, O and ring B = benzo where benzo is substituted by benzo. The substituted benzo represents E=phenyl and R4=H of the instant application.

The closest definition found in the Specification of 10/500,096 regarding the term "benzo" is found on page 6 of its Specification where the term phenylcarbonyl radical corresponds to benzoyl radical. In essence, 10/500,096 equates the term benzo to mean phenyl. In the chemical community, the term "benzo" is commonly referred and related to the term "phenyl".

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only.

For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John Mabry, PhD whose telephone number is (571) 270-1967. The examiner can normally be reached on M-F from 9am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's primary examiner can be reached at (571) 272-0684, first, or the Examiner's supervisor, Janet Andres, PhD, can be reached at (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/John Mabry/
Examiner
Art Unit 1625

/Rita J. Desai/
Primary Examiner, Art Unit 1625